REMARKS

Reconsideration is requested.

Claims 1-16, 33-41 and 43-50 are pending. The claims have been revised, without prejudice. Support for the amendments may be found throughout the specification. Claim 1 has been revised, for example, to include the lower aspect of the range recited in claim 3 and claim 10 has been revised, for example, to include the lower aspect of the range recited in claim 12. No new matter has been added. Entry of the above amendments is requested to at least obviate the Section 102 rejection based on Field et al (U.S. Patent No. 6,593,140) and reduce this issue for appeal.

The Examiner's comments regarding listing of a Search Report on the face of a U.S. patent and the Examiner's acknowledgement of consideration of the Search Report are noted. See page 3 of the Office Action dated January 5, 2010.

The Examiner is requested to see the following excerpt from advice available on the Patent Office web site under "On Line Chat Transcripts" available at http://www.uspto.gov/inventors/independent/chats/faq/transcriptsf_m.jsp on March 4, 2010:

> **International Search Report**
>
> **Should you file an information disclosure statement if you receive an international search report, and should you simply file the whole report? Should you list it on SB08B as a non-patent literature document?**
>
> Yes, you should file your international search report in an IDS. It should be listed on the PTO/SB/08 http://www.uspto.gov/web/forms/index.xml;/forms/index.jsp or PTO-1449. See MPEP 609.04(a) http://www.uspto.gov/web/offices/pac/mpep/index.htm;http://www.uspto.gov/web/offices/pac/mpep/index.htm

The following similar advice was provided by the Patent Office in an "On Live Chat for Independent Inventors (22FEB2006) :

teachme (Feb 22, 2006 2:44:14 PM)
should you file an information disclosure statement if you receive an international search report, and should you simply file the whole report? Should you list it on SB08B as a non-patent literature document?

USPTO Expert (Feb 22, 2006 2:46:20 PM) **EDITED ANSWER**
Teach me - yes, you should file your international search report in an IDS. It should be listed on the PTO/SB/08 http://www.uspto.gov/web/forms/index.jsp (forms/index.jsp) or PTO-1449. See MPEP 609.04(a) http://www.uspto.gov/web/offices/pac/mpep/index.htm (http://www.uspto.gov/web/offices/pac/mpep/index.htm)

The applicants have therefore followed the Patent Office advice with regard to listing the International Search Report on an art statement for the Examiner to acknowledge consideration of same. Similar advice from the Patent Office would presumably be received with regard to Search Reports from foreign patent offices.

The Remarks of the Amendment filed October 2, 2009, demonstrate an accepted practice of the Patent Office and patent applicants. Rule 56 encourages the applicants to cite "information" as opposed to merely publications as appears to be suggested by the Examiner's comments on page 3 of the Office Action dated January 5, 2010. Rule 98 similarly refers to listing of "all patents, publications, applications, or other information submitted for consideration by the Office".

MPEP § 2001.04 provides the following:

> The term "information" is intended to be all encompassing, similar to the scope of the term as discussed with respect to 37 CFR 1.291(a) (see MPEP § 1901.02). 37 CFR 1.56(a) also states: "The Office encourages applicants to carefully examine: (1) prior art cited in search reports of a foreign patent office in a counterpart application, and (2) the closest information over which individuals associated with the filing or prosecution of a patent application believe any pending claim patentably defines, to make sure that any material

> information contained therein is disclosed to the Office." The sentence does not create any new duty for applicants, but is placed in the text of the rule as helpful guidance to individuals who file and prosecute patent applications.

Return of a completely initialed copy of the previously-filed PTO 1449 Form as acknowledgement of consideration of the listed Information Disclosure Statement and assurance same will be listed on the first page of any patent issuing from the present application is again requested.

The objections to claims 1 and 10 is obviated by the above amendments. Entry of the present Amendment and withdrawal of the objection is requested.

To the extent not obviated by the above amendments, the Section 102 rejection of claims 1, 4-11, 14-16, 33, 34, 37-41, 43 and 46-50 over Field et al (U.S. Patent No. 6,593,140) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following comments.

Field describes culture of myeloma cells at 0.2 mg/L ferric ammonium citrate, which is not included in the above claims. The reference fails to teach each and every aspect of the claims. Withdrawal of the Section 102 rejection over Field et al is requested.

The applicants further note that Field et al demonstrate *culture* of myeloma cells in a medium with a low iron concentration and in the absence of chelators and transferrin but it is disputed that Field et al demonstrate the *growth* of myeloma cells in such a medium. As the Examiner points out, the disclosure of Field et al states that the

cells do not survive after 48 hours. The claims however require growth of the inoculated culture medium which is defined on page 11, lines 19-25 of the application as

> "the continuous growth of the cells over multiple subcultures with at least a doubling and preferably a tripling in cell number at each passage, i.e. from one subculture to the next".

Entry of the above amendments and withdrawal of the Section 102 rejection over Field et al are requested.

To the extent not obviated by the above amendments, the Section 102 rejection of claims 1-7, 33-41 and 43-50 over Gorfien et al (U.S. Patent Application Publication No. 2006/0148074) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following further comments.

The applicants believe that the teachings of Gorfien are not relevant to the presently claimed invention. The Examiner has characterized the reference as teaching that

> "Myeloma cells were cultured *in vitro* in suspension culture in media lacking transferring [sic], lipophilic chelators and nitrogen containing chelators but in the presence of ferric chloride-sodium citrate". See page 5 of the Office Action dated January 5, 2010.

Gorfien does not exemplify the growth of myeloma cells in a medium containing iron as defined in the claims. The applicants understand the figures of Gorfien et al. to illustrate only the culture and growth of CHO and 293 cells and in ¶ [0148] Gorfien states that the preferred cells for cultivation using the medium defined are mammalian

epithelial cells. It is stated in ¶ [0153] that the medium can be used to grow hybridoma and myeloma cells – but there is no exemplification of this.

Claim 1 of the present application requires that growth of the inoculated culture medium is using **agitated** suspension culture. Gorfien states at the end of ¶ [0166] that

> "agitation of the media and the suspended cells will be minimized to avoid denaturation of media components and shearing of the cells during cultivation".

Gorfien therefore does not teach all of the required features of claim 1 of the present application and is therefore not detrimental to the novelty thereof.

Withdrawal of the Section 102 rejection over Gorfien is requested.

To the extent not obviated by the above amendments, the Section 103 rejection of claims 1-16, 33-41 and 43-50 over Field et al (U.S. Patent No. 6,593,140) in view of Gorfien et al (U.S. Patent Application Publication No. 2006/0148074) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following comments.

The Examiner asserts that

> "It would have been obvious to one of ordinary skill in the art at the time of the invention was made to use ferric ammonium citrate as taught by Field et al in the media taught by Gorfien et al because Gorfien et al teach that it is within the ordinary skill of the art to use particular levels of iron to culture myeloma cells and because Gorfien et al teach that it is within the ordinary skill of the art to use ferric ammonium citrate as a source of iron." See page 6 of the Office Action dated January 5, 2010.

Field and Gorfien can not be considered in isolation as one of ordinary skill in the art is informed by the whole of the art available at the time this application was filed.

The applicants believe that this is especially important when the body of art teaches away from an claimed invention, as is the case with the present application.

Furthermore, the applicants believe that the Examiner has read more into the disclosures of Field and Gorfien than is actually provided therein. As previously discussed, Field et al teach specifically that ferric ammonium citrate at the concentrations currently claimed does not support the growth of myeloma cells in the absence of either transferrin or the chelator tropolone. Thus, although Field may teach that ferric ammonium citrate can "provide a viable source of iron supplement" (Office Action dated January 5, 2010, page 8, last 2 lines) that is only the case when either transferrin or tropolone is present. The teaching that ferric ammonium citrate can be used as an iron source cannot be separated from the requirement that transferrin or tropolone be present for this to be the case.

The Examiner states that the requirement of Gorfien is only with regard to the concentration of the iron. This statement is believed to illustrate the Examiner's belief that chelated iron and free iron are interchangeable in the culture of mammalian cells, specifically myeloma cells. However the body of art available at the time of filing of this application illustrates that this simply is not the case.

Gorfien exemplifies only CHO and 293 cells. It is noted that a medium that allows culture of CHO cells, for example, will not necessarily also allow culture of myeloma cells. This is illustrated in Keen et al., U.S. Patent No. 5,633,162 (which is a continuation of the application which issued as U.S. Patent No. 5,316,938 (of record))

discussed in the background to this application, who demonstrated that ferric citrate, ferrous sulphate and ferric ammonium citrate can be used at concentrations of between 0.25 and 5 mg/L to replace transferrin in the culture of CHO cells. This is in agreement with the teachings of Gorfien. Similarly, Ramos et al in WO 92/05246 (of record) report that in the cultivation of epithelial cells, in particular CHO cells transferrin can be replaced with ferric citrate at 0.6 – 16 mg/L iron. However, Ramos also states that that medium was not suitable for the culture of myeloma cell lines. Neumannova et al (In vitro Cell Dev. Biol. 31:625-632 (1995) (of record)), also cited in the background to this application, furthermore demonstrated that myeloma cells were incapable of growing in media containing iron in the form of ferric citrate at concentrations of 1.25 mg/L.

Thus, the person ordinarily skilled in the art would reasonably conclude from the above that the requirements of CHO and myeloma cells are different with regard to the provision of iron.

Gorfien do nothing to prove the conclusions of Ramos and Neumannova incorrect. There is no enabling disclosure in Gorfien of the culture and growth under agitated suspension conditions of myeloma cells where the iron is provided in the absence of transferrin or a chelator. Gorfien only exemplifies the growth of CHO and 293 cells. In fact, it is not apparent whether Gorfien exemplify the growth of CHO cells in $FeCl_3$ sodium citrate – the CD CHO medium defined in ¶ [0182] has "a Fe^{2+} and/or Fe^{3+} chelate" added and it is this medium which is used in Example 7-14. It is not apparent from these examples whether the iron is provided by an $FeCl_3$ sodium citrate

chelate or an $FeSO_4$-EDTA chelate. Figure 2 discloses that 293 cells grow equally well in a medium with an $FeCl_3$ sodium citrate chelate or an $FeSO_4$-EDTA chelate, but this cannot be extrapolated to mean that either CHO or any other cell type would also do so. From the available body of art, the ordinarily skilled person would have been led to believe that the results of Gorfien et al were likely to have been obtained using an $FeSO_4$-EDTA chelate. This then concurs with the findings of Field et al, i.e. that a chelator is required in the absence of transferrin.

For completeness, the applicants note that the art at the time of filing of this application makes it clear that the ability of cells to make optimal use of the iron when grown in agitated suspension culture is different from that in static culture.

As no growth of myeloma cells in media containing either an $FeCl_3$ sodium citrate chelate or an $FeSO_4$-EDTA chelate is exemplified in Gorfien, the ordinarily skilled person would not consider combination with the disclosure of Field et al which shows no growth of myeloma cells at the currently claimed amounts of iron in the absence of a chelator or transferrin.

Accordingly, the presently claimed embodiments are inventive over Field and Gorfien, either alone or in combination and withdrawal of the Section 103 rejection is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required.

Respectfully submitted,

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